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(57) Abstract

High molecular weight glucose polymer fraction of starch hydrolysate having a degree of polymerization of 10 to 40, obtained by separating same from such hydrolysate. This fraction has low osmolarity, it is rapidly absorbed by the gut and it has other nutritional advantages. The fraction can be produced from selected corn starch or the hydrolysate can be produced from selected corn starch or the hydrolysate can be treated to favor glucose polymers of 1-4 alpha linkages or 1-6 alpha linkages. Complete dietary products can be made having high caloric content without causing diarrhea. It can be in solid or liquid form, it can be ingested orally or administrated by nasogastric or abdominal ostéotomy means, and preparations containing it in combination with proteins and/or protein hydrolysates may be heated for sterilization with reduced objectionable browning due to the Maillard reaction.

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GLUCOSE POLYMERS AND METHOD OF PRODUCING SAME

CROSS-REFERENCE TO RELATED APPLICATION:

This application is a continuation-in-part of our co-pending application Serial No. 249,647 filed March 31, 1981 entitled "Glucose Polymers and Method of Producing Same."

BACKGROUND OF THE INVENTION:

1. Field of the Invention.

This invention relates to glucose polymers which are useful for the nourishment via the gastrointestinal tract of patients, who, on account of a variety of coexisting medical and/or surgical disorders are not able to eat sufficient food to maintain their nutritional state.

More particularly the invention relates to a new process and product wherein long chain glucose polymers have been produced by the fractionation of a hydrolysate of corn starch. The said material consists of glucose polymers composed of 10-40 glucose units linked by 1-4 alpha and 1-6 alpha-D-glycosidic chemical bonds. The invention also contemplates treating such glucose polymers, or selecting the source material, to provide glucose polymers of the stated degree of polymerization which have enhanced 1-4 alpha linkages and diminished 1-6 alpha linkages.

2. Description of the Prior Art.

The use of shorter chain glucose polymers for nutritional purposes is well known. The use of oligosaccharides which are glucose polymers of short chain length for intravenous injection has been proposed. Among prior patents in this regard are the following: Ramsey et al., U.S. Patent 4,182,756 provides glucose polymers having an average degree of polymerization (DP) of 4 to 10 in intravenous solution. A profile of the glucose polymers

employed for this purpose is described in that patent at column 4, lines 59 to 65, as follows:

> "According to the present invention, it has been found that a glucose polymer mixture having at least 99% of its molecules less than 26 glucose units, at least 85% of its molecules less than 11 glucose units and at least 20% of its molecules less than 4 glucose units can be utilized by a human patient when intravenously administered by a peripheral vein of the patient."

Milner, U.S. Patent 3,928,135, relates primarily to preparations of glucose polymers intended for intravenous injection and is limited to starch sources containing not more than 20% amylopectin because of the lack of enzymes in the blood which are capable of breaking down amylopectins. The glucose polymers of the Milner patent, when used for intravenous injection, are said to contain not more than 10 glucose units. The mixture does, however, contain substantial proportions of glucose and maltose. As stated in this patent at column 4, lines 22-30,

> "The invention also includes the novel glucose polymers that are suitable for intravenous use which comprise a mixture of polymers each of which is substantially no more than 10 glucose units long. The difference between this intravenous product and the oral product is that the oral product also contains a proportion, e.g., 10% by weight of polymers more than 10 glucose units long, and may have present an unspecified number of 1-6 linked units."

McKay U.S. Patent No. 4,021,543 relates to the utilization of glucose polymers having an average short chain length of about 3 to 8 units in an oral electrolyte solution wherein the unpleasant taste of saline is substantially reduced and simultaneously affording an increased caloric intake.

Formulated hospital diets indicated specifically for patients who have difficulty in eating or digesting normal foods have been developed to provide high biological value proteins, carbohydrates, fats, minerals, and vitamins. These complete foods have formulas of widely variable values with respect to ingredients which affect viscosity, osmolarity, and taste, to mention a few.

One critical factor which determines the value of formulated enteral feeding solutions is the inherent osmolarity. Osmolarity is a function of the number of individual ions per unit of solution. Osmotic pressure gradients are established across the membranes of cells lining the intestinal lumen. If the tonicity of the fed solution is high, water will cross from inside the cell and between cells to dilute the hypertonic solution. Thus, the lumen becomes filled with water, and this net efflux of water alone will result in filling the lumen and causing diarrhea.

The foregoing knowledge aids those skilled in the art to administer for nourishment of patients low residue liquid diets that have an osmolarity as near as possible to that of circulating blood plasma. Because existing average short-chain length glucose polymer energy sources used in these diets exert a relatively high osmotic pressure, only relatively small quantities per unit volume can be used in these diets.

SUMMARY OF THE INVENTION:

Prior to this invention, purified long chain glucose polymers have not been utilized for the nourishment of patients. The advantages of the present invention are that the long chain glucose polymer material is rendered soluble, the exerted osmotic pressure is lower, and the caloric content higher than the existing average short chain length glucose polymers presently in use and described above.

Additional advantages of the present invention are that the long chain length glucose polymers have unexpectedly favorable digestion and absorption properties, thereby improving the kinetics of the resulting glucose adsorption in the human intestine. These characteristics of the product provide efficient adsorption of fluid and electrolytes. On account of these properties the product can be administered to patients with abnormalities of digestive and adsorptive functions as well as those with normal gastrointestinal function. A further advantage is that the long chain length glucose polymers have favorable taste and processing properties. In spite of their long chain length these polymers do not appreciably increase the viscosity of products to which they are added.

Yet a further advantage of the DP 10-40 mixture is that it has a considerably lower reducing sugar content than glucose and short chain glucose polymers whereby the phenomenon of browning or the Maillard reaction does not occur or occurs in much diminished degree during the customary heat treatment of canning and sterilizing operations. This property renders fluid products using whole proteins or protein hydrolysate whiter (which therefore simulates whole milk) when processed through a high temperature sterilizer.

Difficulties with preparations intended for intravenous use are apparent. The product must be sterile, it must be free of particulate matter, it must be free of pyrogens, and it must be substantially free of glucose polymers which cannot be depolymerized by enzymes in the blood. The preparation of such a material is laborious and time-consuming and its administration requires medical skill and is hazardous unless employed with care and the proper equipment.

By way of contrast, carbohydrates taken enterally (either by mouth, by nasogastric feeding techniques or if needed, by an abdominal ostomy) need not be sterile but only sanitary within the general requirements of food. These carbohydrates need not be free of pyrogens, and they need not be free of amylopectin. Heretofore, as far as we know, no one has formulated a carbohydrate which can be administered orally or ingested actually as described above which has such a favorable caloric content and low osmotic pressure and such favorable absorptive properties to make it compatible for use in clinical conditions where there is either abnormal gastrointestinal function or reduced luminal hydrolysis (exocrine pancreatic insufficiency) or conditions in which there is loss of small intestinal absorptive capacity.

It is an object of the present invention to provide a carbohydrate formulation to be taken enterally either by mouth or nasogastric means or by an abdominal ostomy which is characterized by satisfactory digestive and absorptive properties and does not give rise to hypertonicity.

The above and other objects of the invention will be apparent from the ensuing description and the appended claims.

DETAILED DESCRIPTION OF THE INVENTION:

We have discovered a certain fraction of glucose polymers resulting from a process for the hydrolysis of starch that is useful and advantageous. The fraction consists predominantly of glucose polymers having glucose chain lengths of 10 to 40 glucose units with negligible amounts of glucose, maltose and glucose polymers having a chain length of less than 10 units. Unexpectedly, the fraction is satisfactorily digested and absorbed in the absence of luminal alpha-amylase activity and is therefore advantageous in cases of pancreatic malfunction where sufficient amounts of the enzyme amylase is lacking. In the presence of pancreatic amylase the fraction exhibits advantageous absorptive properties since glucose derived from the fraction's digestion is absorbed faster than when free glucose is presented for absorption to the cells lining the gut. Consequently, the long chain length glucose polymers are particularly advantageous for those persons having normal pancreatic function. As will be shown, the long chain length glucose polymers have a further unexpected and substantial stimulating effect on water and electrolyte absorption making them particularly advantageous for those patients who suffer from diarrhea that results from excessive water and electrolyte secretion, however induced.

It is an advantage of the said process for producing the average long chain length glucose polymer product that when it is desirable to maximize the rate of intestinal absorption of glucose following enteral administration, for example when gastrointestinal function is normal, the ratio of 1-6 alpha:1-4 alpha-D-glycosidic bonds can be decreased by selection of the type of corn starch or by incubating the native corn starch with bacterial iso-maltose enzymes which cleave the branched 1-6 alpha-D-glycosidic linkages leaving predominantly 1-4 alpha-D-glycosidically linked long chain length glucose polymers.

The ensuing examples will show that this aspect of the invention produces favorable absorption properties, hitherto not previously described. A suitable process is that described by Morehouse and Day, U.S. Patent No. 3,663,369. In accordance with that patent, corn starch is subjected to hydrolysis by acid or a suitable enzyme to the point of liquefying the starch and to provide an aqueous dispersion which is substantially free of residual starch granules and which has a dextrose equivalent value not substantially above three. This intermediate product is then subjected to a second step in which a dextrinizing enzyme is used to produce a hydrolysate having a dextrose equivalent (D.E.) value not substantially above 18. The hydrolysate of the Morehouse patent contains a more or less continuous profile or spectrum of glucose polymers ranging from polymers having a DP of about 40 down to glucose. For our purposes this hydrolysate is a useful starting material and it may be treated, as illustrated in Example 1, to separate the desired fraction of glucose polymers.

Example 1

A starch hydrolysate prepared in accordance with the Morehouse patent was used as the starting material. It contained a small quantity of glucose and maltose (e.g., less than 2%). This starch hydrolysate was placed in aqueous solution in a concentration of between 10% and 30%, e.g. 20%, and the solution was pumped into a chamber containing a filter whose passage pore size was such that materials greater than a 2000 molecular weight cannot pass through the membrane. This provided a cut-off sieving of glucose polymers which are approximately 10 glucose units in length.

Two methods were used to accomplish the separation of the two major fractions (one above 10 glucose unit polymer; one below). The fraction above 10 units is the

product of this invention. Fraction I was mainly 3 to 10 glucose units long, and Fraction II was greater than 10 but with most polymer under 30 glucose units long. The first method filters the solution containing the original mixture of solubilized starch past the filter so that the filtrate contains less than 10 glucose unit polymers and the retentate contains the glucose polymers with glucose units greater than 10.

In the second method, which is more efficient and is called the diafiltration method of ultrafiltration, an amount of water is added to the original solution equivalent to that which passes through the filter. This also dilutes the retentate and prevents pile up on the filter and permits larger amounts of lower than G10 material to pass through the filter.

The type of ultrafiltration equipment, the amount of dilution (diafiltration), and the time the material circulates in front of the filter determines the completeness of fractionation of the two groups of polymers. In the method we employed, the low molecular weight Fraction I (short chain polymers under G10) were in the solution at about 1 to 2% solids with less than 2% of the high molecular weight fraction present as a contaminant. By using reverse osmosis, the solution was concentrated to 10% solids. The product was concentrated further by evaporation under vacuum until it was 30% solids. This low molecular weight fraction was then spray dried to a white, fine, highly soluble powder of glucose polymers from 3 to 10 with a dextrose equivalent (D.E.) of about 14 to 15.

The high molecular weight Fraction II was back-flushed off of the filter and placed in a vacuum evaporator, taken to a 40% solids solution and spray dried. The final product contained less than 5 per cent low molecular weight (DP <10) fractions and had a dextrose equivalent of

approximately 4.

Example 2

Fraction II of Example 1 contains long chain glucose polymers that have ratios of 1-6 to 1-4 alpha-D-glycosidic linkages according to the starch used as starting material and according to the effect of acid and enzymatic hydrolysis on these linkages. Desired ratios of these linkages can be provided by selection of the starch or by treating the starch before or after fractionation with bacterial isomaltase enzyme, which selectivity cleaves the 1-6 linkage.

After backflushing the high molecular weight Fraction II of Example 1 off of the filter and concentrating to 30% solids, the pH is adjusted to 7 and the bacterial enzyme isomaltase is added to the solution at a temperature range of 50°C to 95°C. The length of time of the hydrolytic action of the enzyme determines the ratio of 1-6 to 1-4 alpha-D-glycosidically linked long chain length glucose polymers. No simple test is known to measure the exact amounts of 1-6 to 1-4 linkages. However, empirical tests indicative of digestion can be used, such as osmolality. When the desired conversion action is completed, the hydrolysis may be stopped by adjusting the pH to below 4.0 or by heating the mixture above 110°C until the enzyme is inactivated. The longer the enzyme action, the higher the osmolality, indicating more cleavages or hydrolysis. This enzymatically altered product has a greater 1-4 to 1-6 ratio than Fraction II. If desired, it may be subjected to filtration as in Example 1 to separate a Fraction IIA which is substantially free of glucose and glucose polymers having a DP less than 10 which were produced by the enzymatic treatment.

An alternative process avoids having the elevated osmolality in the final product and the need for a second filtration. In this alternative, the hydrolysate that constituted the starting material of Example 1 is treated with isomaltase to cleave 1-6 linkages and the material is then subjected to filtration as in Example 1. Fraction IIB resulting from this procedure consists predominantly of glucose polymers of DP 10 or more but with a greater ratio of 1-4 to 1-6 linkages than Fraction II.

It is of interest to note that corn starch hydrolysates in common use that have a D.E. below 5 are reported to be "cloudy in solution" and add viscosity to products in which they are incorporated. The products of this invention are useful in making clear solutions and does not add appreciable viscosity to products.

The following are examples illustrating certain useful properties of the glucose polymers of the invention:

Example 3

The composition of average long chain length glucose polymers presently utilized in hospital diets as determined by high pressure liquid chromatography is shown in Table I. Approximately 51% of the total glucose content is contained in the G10-G40 fraction with 34% in the G4-G10 fraction and 14% contained as maltrotriose (G3), maltose (G2) and free glucose (G1). (The letter "G" signifies a single glucose unit.)

Table I

Glucose Chain Length (G1-G40)	Total Glucose Content %
G10 - G40	51.5
G4 - G10	37.7
G3	7.3 ± 0.2
G2	4.1 ± 0.1
G1	2.4 ± 0.3

A typical composition of the liquid of the present invention as determined by high pressure liquid chromatography is in Table II.

Table II

Glucose Chain Length (G1-G40)	Total Glucose Content %
G10 - G40	95
G4 - G10	4
G3	trace
G2	trace
G1	trace

Example 4

The osmolality of the product shown in Table II, determined by the freezing point depression method, is shown below in Table III and is compared with glucose, maltose, Caloreen (trademark of a product of Roussel Laboratories, Ltd., Wembley, London, U.K.), and a maltodextrin contained in and sold as Vivonex by Morton-Norwich. The Caloreen is said to contain an average glucose chain length of 5 units. The Vivonex is said to contain an average glucose chain length of 5 units based upon a dextrose equivalent of 20.

Table III

Glucose Polymer Source (100 g/kg water)	Osmolality (milliosmols/kg) (Freezing Point Depression)
Glucose	569 (derived from Geigy Scientific Tables)
Maltose	270
Caloreen	92
Maltodextrin (Vivonex)	104
Long chain glucose polymer of this invention	18

Table III shows that the long chain polymers of this invention exert a substantially lower osmotic pressure than any of the other sources of glucose polymers, including the average short chain length glucose polymers of the type used as the carbohydrate energy source of present low residue liquid nutritional diets.

Example 5

One of the critical factors which determine the value of formulated enteral feeding solutions, namely, the inherent osmolarity, will be considerably improved if the said long chain glucose polymer product is utilized as the carbohydrate source. This is so because on a caloric per fluid unit basis the product of this invention exerts a substantially reduced osmotic pressure compared to control formulations. In this way, if equicaloric amounts of the invented products are used for enteral feeding, the upper gut lumen will become filled with less water, thereby reducing diarrhea.

A second critical factor which determines the value of formulated enteral feeding solutions is the kinetics

of digestion and transport across the intestinal mucosa which result from the chemical form of the nutrients. The absorptive properties of the long chain glucose polymer of this invention were investigated in the jejunum of normal human subjects using an in vivo steady state segmental perfusion technique as described in the journal GUT, Volume 11, page 947, 1970. Luminal alpha-amylase was therefore excluded from the 25 cm segment of jejunum studied by means of an occlusive balloon described in the cited reference. Sugar-saline solutions with a measured osmolality of 285-295 mOsm/Kg, and a nonabsorbable marker (polyethylene glycol 4000) were infused at 20 ml/minute. The test solution containing the long chain glucose polymer product of the invention yielded 140 mmol/L glucose after complete hydrolysis. Suitable control solutions containing glucose and containing the aforesaid maltodextrin glucose polymer mixture of the elemental diet Vivonex, both yielding 140 mmol/L free glucose after complete hydrolysis, were also perfused as shown in Table IV.

Table IV

Test Solution	Glucose Content after complete hydrolysis mmol/L	Glucose Absorption mmols/hr/25 cm
Product of invention (Fraction II)	140	31.5 ± 3.8
Fraction I	140	51.9 ± 5.4
Maltodextrin	140	49.5 ± 7.4
Glucose	140	72.6 ± 8.9

Bearing in mind that the product of the invention had very little G4 to G10 glucose oligomers and only traces of glucose, maltose and triose, it is evident from Table IV that glucose absorption from Fraction II occurs quite satisfactorily notwithstanding the fact that the product was

of high molecular weight. The high molecular weight polymers of the invention result in efficient brush border intestinal hydrolysis, therefore they can be efficiently utilized by patients with pancreatic malfunctions who have a reduced luminal amylase activity.

Since the perfusion technique that was employed occuled pancreatic amylase activity from the segment of intestine studied, it is apparent that only digestive enzymes normally in the brush border sufficed for the very satisfactory breakdown of the long glucose chains, i.e., pancreatic alpha amylase activity was unnecessary. At the same time the osmolality of the fluids in the test section of the intestine was much lower; see Table III. The higher rate of absorption of the maltodextrin product and of Fraction I was to be expected because of the much lower average molecular weight of the glucose polymers. Any advantage of this high rate of absorption is more than offset by the greatly diminished osmolality of the product of the invention.

The absorptive properties of the long chain length glucose polymers in patients with normal pancreatic function were investigated by hydrolyzing the product of the invention to completion in vitro with pancreatic alpha-amylase and studying glucose absorption using the same experimental technique. The results were as follows:

Table V

Test Solution	Glucose Content after complete hydrolysis	Glucose Absorption mmols/hr/25 cm
100% alpha-amylase digested product of the invention	140	49.8 ± 7.6
Unhydrolyzed product of the invention (for comparison)	140	31.5 ± 3.8
Glucose	140	41.4 ± 6.5

As can be seen, the specially formulated long chain length glucose polymers of the present invention, when hydrolyzed with pancreatic alpha-amylase compare favorably with glucose as to the transport kinetics across the intestinal mucosa. Thus a hitherto undescribed finding is that the product of the invention, under circumstances of normal gastrointestinal function, actually exerts a kinetic absorption equal to or perhaps slightly greater than glucose absorption, further illustrating the advantages of using such products as this is accomplished with greatly diminished osmolality.

Example 6

An additional critical factor that determines the value of formulated enteral feeding solutions is the ability of the administered nutrients to stimulate fluid and electrolyte absorption from the lumen of the human small intestine. Experiments were performed to investigate and compare the fluid and electrolyte absorption from isotonic solutions of glucose and the alpha-amylase digest of the long chain length glucose polymers of the invention. The results were as follows:

Table VI

Test Solution	Glucose Content after complete hydrolysis	Sodium Absorption mmol/hr/25 cm	Water Absorption ml/hr/25 cm
Alpha-amylase digested product of the invention	140	16.4	95.5 ± 25
Glucose	140	-0.1	85.3 ± 36

These experiments illustrate the advantages which the long chain length glucose polymers in the digested form exhibit in terms of their marked stimulating effects on fluid and

electrolyte absorption. The product of the invention therefore not only exerts a low osmotic pressure and improves the transport kinetics across the intestinal mucosa, but also acts as a powerful stimulant to fluid and electrolyte absorption in the human intestine. For persons with normal pancreatic function and for persons with abnormal pancreatic function a nutrient is provided which contributes a larger caloric intake per unit osmotic pressure as compared to average short chain glucose polymers or dextrose without the adverse effects caused by the osmotic pressure difference.

The following are examples of typical formulations for various products which can be made using the high molecular weight or long chain glucose polymer of the invention:

Example 7

A whole protein, lactose-free, complete dietary food with a low osmolarity in a rotary-retort sterilized can is provided as follows. This product is intended primarily as a tube diet fed via the nasogastric route.

Component	Percentage
Water	78.3
Protein as calcium caseinate and soy protein isolate	4.0
Long chain glucose polymer	13.0
Corn and soy oil	3.25

Also added are quantities of vitamins and minerals to meet the Recommended Daily Allowances of the National Research Council. This product had the following analytical results in proximate analysis (w/v):

Protein	-	34.8 g/L.
Fat	-	34.8 g/L.
CHO	-	136.0 g/L.
Ash	-	5.5 g/L.

Osmolarity was 348 mOsm/L.

Example 8

The protein source of this (a dry mix to be reconstituted with water) is a lactalbumin hydrolysate consisting primarily of di- and tri-peptides with 20% free amino acids. In this case, the glucose polymer is sprayed with a mixture/emulsion containing the oil, emulsifiers, and fat-soluble vitamins. The dry and coated powders are then blended.

Ingredient	% w/w
Oligopeptide (lactalbumin)	19.0
Long chain glucose polymer	74.2
Soy and medium chain triglyceride oil	4.4
Lecithin and Tween 80	0.3
Vitamin and mineral mix	2.1
	100.0

This product reconstitutes to a clear solution with a stable emulsion and had a 480 mOsm/L. osmolarity.

Example 9

(a) As noted above certain glucose polymers are known to have higher 1-6 to 1-4 alpha-D-glycosidic bonds than others. They are digested more slowly when presented to the brush border of the normal human gut while occluding pancreatic enzymes. Isomaltase enzymes, whose function it is to cleave 1-6 bonds, are secreted at the brush border of

the cells lining the mammalian gut. Heretofore, it was not observed that this enzyme is either limited in its rate of reaction or that the quantity secreted is limited when compared with substrate 1-6 linkages.

We have found that glucose polymers of G10 or greater with all of their advantages of digestibility and enhanced transport of electrolytes and water as shown above can be selected to have a relatively high 1-6 to 1-4 linkage ratio and, thereby, their digestion and resulting glucose transport can be significantly slowed. This property of selective digestion rate is of value, for example, in feeding patients who are in need of tube feedings from gastrointestinal disease, such as described above, but who are also diabetic, for example. In these cases, it is of considerable value to be able to feed a carbohydrate that is "programmed" to transport glucose slowly from the lumen, through the intestinal wall, to the serosal side and thereby not present a plasma glucose peak but provide a low but steady rate of infusion of glucose thereby diminishing glucose's insulin-stimulating effect. This example further illustrates the value and medical properties of the greater than 10 glucose unit polymer of this invention.

(b) Conversely, when it is desirable to feed carbohydrate at a rapid rate, for example, to a patient who has been burned and needs a high caloric intake to survive, it is possible to produce a glucose polymer of greater than G10 that has low 1-6 to 1-4 alpha-D-glycosidic bonds. Here, the caloric density combined with tolerable osmolarity and rapid transport gives a set of properties highly desirable for a tube diet for trauma or severely catabolic patients.

High 1-6 to 1-4 ratio polymers as in Example 9 (a) can be provided by selection of a starch having such proportions and proceeding as in Example 1. High 1-4 to 1-6 ratio polymers as in Example 9 (b) can be provided as in

Example 2.

The high 1-6 to 1-4 ratio polymers of Example 9 (a) and the high 1-4 to 1-6 ratio polymers of Example 9 (b) may be formulated as in appropriate examples above.

An added and important advantage of the glucose preparation of the present invention, when prepared by the procedure of Example 1 including the step of ultrafiltration, is that when formulated as in Examples 7 and 8 to provide complete formulations, the formulations are much more stable on storage and do not stratify, separate or form gels on standing as do other similar formulations containing other glucose polymers. This is illustrated by the table below:

	(1)		(2)	(3)	(4)	(5)	(6)
Formulation		Polymer	Ca	Mg	Na	P	Stability Duration Days
I	(a)	Polymer of present invention containing predominantly glucose polymers having a degree of polymerization of 10 to 40	59	21	205	10	600
II	(b)	50/50 mixture of (weight basis) of glucose polymers of (i) 2 to 10 degree of polymerization and (ii) 10 to 40 degree of polymerization	240	100	805	74	90
III	(c)	Polymer prepared by the method of Morehouse U.S. Patent 3,663,369, 1st stage	244	47	886	74	30

The figures in Columns (2) to (5) are parts per million of the elements indicated. Formulations I, II and III were

prepared identically except that Formulation I contained polymer (a), Formulation II contained polymer (b) and Formulation III contained polymer (c) as the carbohydrate component. The other components of each formulation were standard ingredients (protein, lipid, vitamins and minerals) used in a complete dietary formula.

Polymer (a) was prepared as in Example 1, which was Fraction II (predominantly glucose polymers of 10 to 40 degrees of polymerization) and had been produced as retentate in ultrafiltration. The low content of calcium, magnesium, sodium and phosphorus was due to the fact that the corresponding salts diffused through the filter medium into the filtrate. Polymer (b) contained the mineral content of the 2-10 DP component. Polymer (c) was prepared as in Morehouse U.S. Patent No. 3,663,369, first stage; i.e., by treatment of starch with acid or enzyme to provide a liquid product free from residual starch but having a low dextrose equivalent. This polymer as produced for purposes of the present invention, consisted primarily of glucose polymers having a degree of polymerization of 10 to 40, but it also contained the mineral content of the starch and resulted, when formulated as Formulation III, in an unstable product.

Formulations I, II and III may be typically as described in Examples 7 and 8.

The foregoing invention can now be practiced by those skilled in the art. Such skilled persons will know that the invention is not necessarily restricted to the particular embodiments herein. The scope of the invention is to be defined by terms of the following claims as given meaning by the preceding description.

WHAT IS CLAIMED IS:

1. A glucose polymer preparation in which the glucose polymers consist predominantly of those polymers having a degree of polymerization of 10-40 with no substantial quantities of lower polymers.

2. The preparation of Claim 1 wherein the proportion of polymers below 10 and of glucose and of maltose does not exceed about 10% and the proportion of glucose polymers having a degree of polymerization in excess of 30 does not exceed about 15%, such percentages being by weight based upon the total weight of glucose and glucose polymers.

3. The glucose polymer preparation of Claim 2 in the form of an aqueous solution.

4. The glucose polymer preparation of Claim 2 in the form of a dry material which can be reconstituted by the addition of water.

5. The glucose polymer of Claim 2 or 3 which has a mineral content sufficiently low that when formulated with protein and other nutrients a product with a stable emulsion results.

6. The glucose polymer preparation of Claim 2 or 5 in admixture with a proteinaceous component and a lipid component, such protein component being one or more of whole protein ingredient, polypeptide ingredient and amino acid ingredient, along with vitamins and minerals.

7. The preparation of Claim 6 in the form of an aqueous solution.

8. The preparation of Claim 6 in the form of a dry material which can be reconstituted by adding water.

9. A nutrient material suitable for ingestion by a person having pancreatic malfunction, said material containing as a principal caloric component, and as its substantially sole carbohydrate component, a fraction of glucose polymers defined as in Claim 1 or 5, which are capable of transport at the brush border of the small intestine.

10. The nutrient material of Claim 9 in aqueous solution suitable for enteric ingestion.

11. The nutrient material of Claim 9 in solid form capable of being reconstituted by the addition of water.

12. A glucose preparation as in Claim 1 or 5 in which 1-4 alpha linkages predominate over 1-6 alpha linkages.

13. The glucose preparation of Claim 12 wherein such predominance arises from the choice of source material for the glucose polymers.

14. The glucose preparation of Claim 12 wherein such predominance arises from the fact that hydrolysate of the source material has been treated enzymatically to selectively cleave 1-6 alpha linkage.

15. A glucose polymer preparation as in Claim 1 or 5 in which the 1-6 alpha linkage predominates over the 1-4 alpha linkage.

16. A method of producing a glucose polymer product having a high caloric content coupled with a low osmolality compared to glucose, maltose and triose, said method comprising:

(a) providing a starch hydrolysate containing a mixture of glucose, maltose and higher polymers including polymers of degree of polymerization between 10 and 40, and

(b) separating from such mixture a fraction predominating in those polymers having a degree of polymerization between about 10 and 40 and substantially free of lower and higher polymers.

17. The method of Claim 16 wherein the mixture of polymers of degree of polymerization resulting from step (b) is subjected to enzymatic action to selectively cleave 1-6 alpha leakage and thereby produce a mixture having an enhanced 1-4 to 1-6 ratio.

18. The method of Claim 16 wherein the hydrolysate resulting from step (a) is subjected to enzymatic action to selectively cleave 1-6 alpha linkages and the resulting mixture is then subjected to step (a).

19. The method of Claim 16 wherein the starch which is subjected to hydrolysis step (a) is selected to have a predominance of 1-4 alpha linkages.

20. The method of Claim 16 wherein the starch which is subjected to hydrolysis step (a) is selected to have a predominance of 1-6 alpha linkages.

21. The method of Claim 16 in which separation step (b) is carried out by filtration and the resulting polymers of 10 to 40 degree of polymerization has a much lower mineral content than the starting material.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US82/00390

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.[3] A61K 37/02; C07C 103/52; A61K 31/715; C12P 19/04; C08B 37/00 - U.S.Cl. 260/112R;260/112.5R;424/180;435/99;435/101;

II. FIELDS SEARCHED 536/1

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	260/112R; 260/112.5R; 424/180; 435/99; 435/101; 536/1

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [5]

Chemical Abstracts -- Glucose Polymer Preparation and Use Volumes 66-93

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
Y	US, A, 3,663,369, Published 16 May 1972, Morehouse et al	1-5 and 12-21
Y	US, A, 3,766,165, Published 16 October 1973, Rennhard	1-15
X	US, A, 3,928,135, Published 23 December 1975, Milner	1-21
A	US, A, 4,021,543, Published 3 May 1977, McKay	1-5
X	US, A, 4,182,756, Published 8 January 1980, Ramsay et al	1-21
A,P	US, A, 4,289,688, Published 15 September 1981, Hotta et al	6-8

* Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
30 June 1982	14 JUL 1982
International Searching Authority [1] ISA/US	**Signature of Authorized Officer** [20] Johnnie R. Brown

Form PCT/ISA/210 (second sheet) (October 1981)